UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/998,497	11/30/2001	Paul O.P. Ts'o	214654	6526

23460 7590 12/24/2003

LEYDIG VOIT & MAYER, LTD
TWO PRUDENTIAL PLAZA, SUITE 4900
180 NORTH STETSON AVENUE
CHICAGO, IL 60601-6780

EXAMINER	
OWENS JR, HOWARD V	

ART UNIT	PAPER NUMBER
1623	8

DATE MAILED: 12/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/998,497	TS'O ET AL.	
	Examiner	Art Unit	
	Howard V Owens	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-62* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Response to Restriction Requirement

Upon reconsideration of applicant's remarks and the prior art set forth below, the restriction requirement of claims 1-62 is withdrawn.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1 and 31 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 14 of U.S. Patent No. 5,994,517('517). An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the

reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1 and 31 are merely species to all that is recited in claims 1 and 14 of '517. The instant claims are drawn to a conjugate of a glycosylated peptide that binds to hepatic cell surface receptors; a bifunctional linker which does not contain a naturally occurring amino acid; and a monomer or polymer comprising at least one nucleotide or analog of that inhibits nucleic acid synthesis in a sequence independent manner.

The conjugate of '517 encompasses the three primary components of the conjugate of the instant claims which present a generic conjugate to that which is set forth in the instant claims. In '517, both A portions are drawn to a hepatic carbohydrate ligand; both L portions recite a bifunctional linker that combines the A and P portions in a regiospecific manner. The only difference is that the instant claim excludes naturally occurring amino acids as a bifunctional linker and the P portion inhibits nucleotide synthesis in a sequence independent manner. Since '517 provides for the use of a generic bifunctional linker which connects A and P in a regiospecific manner, it encompasses all compounds that are not naturally occurring amino acids as well; moreover, the oligonucleotide or derivative thereof set forth in '517 encompasses oligonucleotides that inhibit nucleotide synthesis in a sequence independent manner as instantly claimed.

It would have been prima facie obvious to have a conjugate possessing a glycosylated peptide that binds to hepatic cell surface receptors; a bifunctional linker which does not contain a naturally occurring amino acid; and a monomer or polymer comprising at least one nucleotide or analog of that inhibits nucleic acid synthesis in a sequence independent manner.

One of skill in the art would have been motivated to construct a conjugate possessing these components given that the prior art has already set forth these components in a conjugate for the targeted delivery of oligonucleotides.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 2, 11, 16, 19, 20 – 31, 32 and 42 – 54 are rejected under 35 U.S.C. § 102(b), (e) as being anticipated by Ts'o et al., U.S. Patent 5,994,517.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Claims 1, 2, 11, 16, 19, 20 – 32 and 42 – 54 are drawn to a conjugate of a glycosylated peptide (with a pharmaceutically acceptable carrier) that binds to hepatic cell surface receptors; a bifunctional linker which does not contain a naturally occurring amino acid; and a monomer or polymer comprising at least one nucleotide or analog of that inhibits nucleic acid synthesis in a sequence independent manner glycoconjugate wherein a peptide is linked to a nucleotide or analog thereof.

Dependent claims 21 and 43 are drawn to the conjugate of claim 1 further comprising a radioactive nuclide.

Ts'o teaches a conjugate possessing a glycosylated peptide that binds to hepatic cell surface receptors; a bifunctional linker ; and a monomer or polymer comprising at least one nucleotide or analog of that inhibits nucleic acid synthesis in a sequence independent manner glycoconjugate wherein a peptide is linked to a nucleotide or analog thereof (see columns 2-24). Ts'o further teaches the conjugate radio labeled with ^{32}P (col. 25, col. 28-30) and the administration of the conjugates in vivo with saline which constitutes a pharmaceutical carrier.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Claims 1-62 are rejected under 35 U.S.C. § 103(a) as being obvious over Ts'o et al., U.S. Patent 5,994,517 in combination with

Claims 1, 2, 11, 16, 19, 20 – 31 and 42 – 54 are drawn to a conjugate of a glycosylated peptide (with a pharmaceutically acceptable carrier) that binds to hepatic cell surface receptors; a bifunctional linker which does not contain a naturally occurring amino acid; and a monomer or polymer comprising at least one nucleotide or analog of that inhibits nucleic acid synthesis in a sequence independent manner glycoconjugate wherein a peptide is linked to a nucleotide or analog thereof.

Dependent claims 21 and 43 are drawn to the conjugate of claim 1 further comprising a radioactive nuclide.

Dependent claims 3-15, 17, 18 and 32-41 are drawn to the conjugate of claims 1 and 31 wherein the oligonucleotide analog employed as the P portion is an aglycone or 5FdU.

Claims 55-62 are drawn to methods of inhibiting viral replication or abnormal cellular proliferation.

Ts'o teaches a conjugate possessing a glycosylated peptide that binds to hepatic cell surface receptors; a bifunctional linker ; and a monomer or polymer comprising at least one nucleotide or analog of that inhibits nucleic acid synthesis in a sequence independent manner glycoconjugate wherein a peptide is linked to a nucleotide or analog thereof (see columns 2-24). Ts'o further teaches the conjugate radio labeled with ^{32}P (col. 25, col. 28-30) and the administration of the conjugates in vivo with saline which constitutes a pharmaceutical carrier.

Ts'o however does not explicitly teach the use of 5FdU as an aglycone moiety, the sugar modified nucleosides (claims 17 and 18), nor the method of inhibiting abnormal cellular proliferation or viral replication; however, Ts'o teaches that the conjugates may comprise oligodeoxynucleotides containing all 2'-O-modified nucleosides and deoxynucleosides (col.2, line 67 – col.3) which encompasses 5FdU and various sugar modifications.

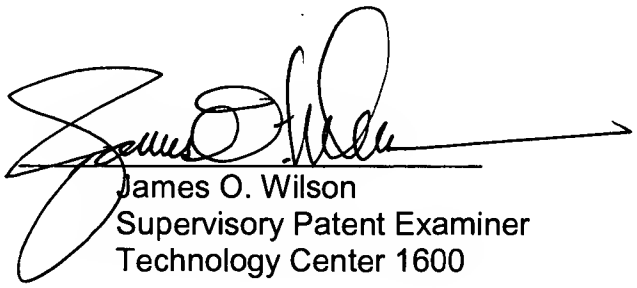
Ts'o does not explicitly teach the use of the compounds of the claimed invention for the inhibition of viral replication or abnormal cellular proliferation; however, Ts'o does state in lieu of the state of the art, that the glycopeptide conjugates comprising hepatocellular recognition ligands (col. 9 – col. 18) are for the delivery of deoxynucleoside analogs into cells and that the advantage of these glycopeptide conjugates is the efficient uptake of the compound by the cell (col.2 and col. 24-32). Ts'o had previously set forth that the state of the art recognizes the delivery of oligo analogs for the inhibition of Herpes and HIV, wherein cellular uptake is important for the activity of the compounds/drugs (col.1, lines 15-35). Wu bridges the nexus for abnormal cellular proliferation or hepatocarcinoma as it teaches that conjugates containing the claimed hepatic ligands can be used to target hepatic receptors for the delivery of chemotherapeutic agents.

It would have been prima facie obvious to use a conjugate possessing a glycosylated peptide that binds to hepatic cell surface receptors; a bifunctional linker which does not contain a naturally occurring amino acid; and a monomer or polymer comprising at least one nucleotide or

analog of that inhibits nucleic acid synthesis in a sequence independent manner for the inhibition of a hepatic viral replication or hepatocarcinoma.

One of skill in the art would have been motivated to use the claimed conjugate for the inhibition of a hepatic viral replication or hepatocarcinoma given as the prior art teaches that conjugates containing carbohydrate hepatic ligands can provide specificity for targeting hepatocytes; moreover, the conjugate provides more efficient uptake and delivery of a targeted drug or compound to the cell.

Howard V. Owens
Patent Examiner
Art Unit 1623



James O. Wilson
Supervisory Patent Examiner
Technology Center 1600

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Howard Owens whose telephone number is (703) 306-4538 . The examiner can normally be reached on Mon.-Fri. from 8:30 a.m. to 5 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the Supervisory Patent Examiner signing this action, James O. Wilson can be reached on (703) 308-4624 . The fax phone number for this Group is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.